Leukaemia Diagnosis Interpretation
All Participants

Participant: 42981 **Trial No: 151603**

Date Issued: 16-November-2015 **Closing Date: 04-December-2015**

Trial Comments

This was an electronic only trial issued to a total of 761 participants. This report replaces version 1.0.0

Your Diagnosis: AML with mutated NPM1

Consensus Diagnosis: AML with myelodysplasia-related changes

Your Diagnosis is classed as a **MAJOR ERROR** result

Performance Score: 50

Running Score: 50

Consensus

	Consensus Diagnosis	Your Diagnosis
Lineage	Myeloid Neoplasms	Myeloid Neoplasms
Subclassification	Acute myeloid leukemias (AMLs) and related precursor n	Acute myeloid leukemias (AMLs) and related precursor n
Diagnosis	AML with myelodysplasia-related changes	AML with mutated NPM1

Breakdown of returned diagnoses

Diagnosis	No Of Returns	Percentage Of Returns
Total Returns	309	100.0
AML without maturation	116	37.5
AML with myelodysplasia-related changes	102	33.0
AML with minimal differentiation	61	19.7
AML with maturation	15	4.9
Acute monoblastic and monocytic leukaemia	4	1.3
Acute myelomonocytic leukaemia	3	1.0
Acute promyelocytic leukaemia with t(15;17)(q22;q12); PML-RARA	2	0.6
Therapy-related myeloid neoplasms	2	0.6
Acute megakaryoblastic leukaemia	1	0.3
T-lymphoblastic lymphoma/leukemia	1	0.3
myelodysplastic/myeloproliferative neoplasms, unclassifiable	1	0.3
AML with mutated NPM1	1	0.3

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Leukaemia Diagnostic Interpretation trial 151603

Case History

A 15 year old male presented to the Accident and Emergency department with a heavy nosebleed and a purpuric rash. He had a previous history within the last 7 days of throat infections and had been treated by the GP for tonsillitis.

Haematological examination revealed the following:

Hb- 74 g/L; WBC- 315.80 x10^9/L; PLT- 124 x10^9/L; RBC- 2.37 x10^12/L; HCT- 0.247 L/L; MCV- 104.2 fL; MCH- 31.2 pg

Immunophenotype

The consensus results for the malignant cells had the following phenotype (consensus percentage expression in brackets – corrected to the nearest whole percent):

Positive antigens – CD7 (72%), CD13 (55%), CD33 (95%), CD34 (96%), CD38 (95%), CD45 (100%), CD117 (94%), HLADR (97%), Myeloperoxidase (87%)

Negative antigens – CD2 (18%), CD3 (0%), cCD3 (0%), CD4 (0%), CD5 (0%), CD10 (0%), CD11b (4%), CD14 (1%), CD15 (2%), CD19 (23%), CD20 (0%), CD56 (0%), CD64 (13%), CD79a (0%), TDT (0%)

Cytogenetics and Molecular genetics

46,XY,del(5)(q12q33) [20]

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Peripheral Blood Morphology

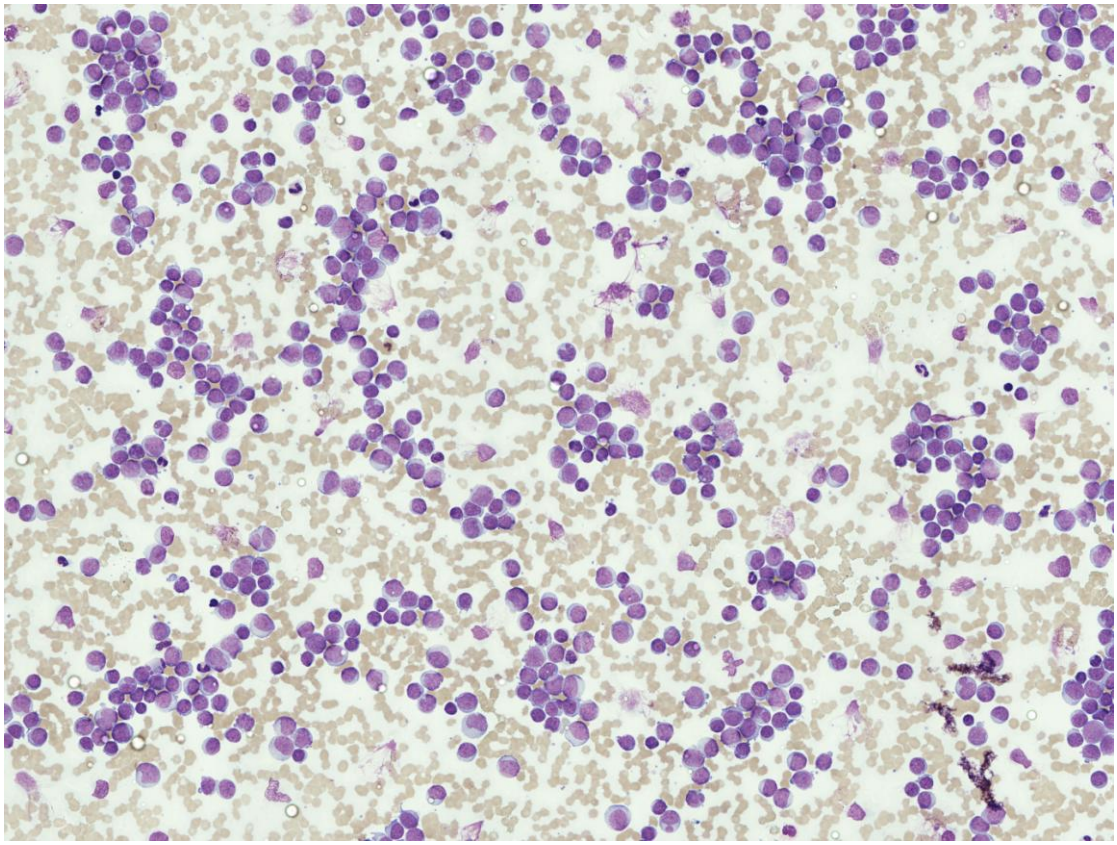
Morphology comments from Professor Wendy Erber
Consultant Haematologist, University of Western Australia, Nedlands, Australia

COMMENT:
The blood film shows a marked leucocytosis with the majority being blast cells. These are pleomorphic, varying in size, nuclear complexity and cytoplasmic granularity. The majority have basophilic or grey-basophilic cytoplasm and immature chromatin with nucleolus. The nuclei vary from round/ovoid to convoluted. Some have small fine granules; Auer rods are not seen. There is minimal differentiation. Thrombocytopenia is noted.

Diagnosis: Morphology is consistent with acute myeloid leukaemia

Examples of Digital Images Issued

Figure 1: Peripheral Blood x50 magnification (May Grünwald Giesma stain)



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EXERCISE CONCLUSION/CASE DISCUSSION

Please note that, because this trial requires a diagnosis based on the WHO guidelines, this report is therefore based on the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th Edition[1].

LEUKAEMIA IMMUNOPHENOTYPING - Part one

All markers show good consensus with respect to the most commonly used manufacturers – Becton Dickenson and Beckman Coulter.

Analysis of CD2, CD13 and CD19 with respect to the fluorochromes used showed wide ranges of results returned. For the 3 antigens mentioned above, the percentage positivity for each fluorochrome ranged from 0% to >70% with no significant differences in overall results seen between the different fluorochromes.

LEUKAEMIA DIAGNOSTIC INTERPRETATION - Part Two

Exercise Consensus Diagnosis (Classified as Correct)

AML with myelodysplasia-related changes

Other Differential Diagnoses (Classified as Minor Errors):

AML without maturation
AML with minimal differentiation
AML with maturation
Acute megakaryoblastic leukaemia
Acute monoblastic and monocytic leukaemia
Acute myelomonocytic leukaemia

Other Differential Diagnoses (Classified as Major Errors):

Acute promyelocytic leukaemia with t(15;17)(q22;q12); PML-RARA
Therapy-related myeloid neoplasms
T-lymphoblastic lymphoma/leukaemia
Myelodysplastic/myeloproliferative neoplasms, unclassifiable
AML with mutated NPM1

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Rationale for Correct Classification

This was an interesting case and clearly gave rise to a variety of conclusions. Firstly, this case was discussed at the recent UK NEQAS LI Steering Committee and it was agreed that any participant that introduced clinical criteria or laboratory data that was not provided in part 2 would be immediately classified as a major error. Please note, that we will always give information that is pertinent to the case involved. Thus, for example, 2 laboratories stated that this case was a therapy-related myeloid neoplasm. For this to be the classified as such there should have been prior cytotoxic chemotherapy and/or radiation therapy administered for a prior neoplastic or non-neoplastic disorder. This was a newly presented case on a 15 year old and with no history of prior treatment. Furthermore, introduction of cytogenetic or molecular abnormalities (e.g. t(15;17)(q22;q12) (by two individuals) and NPM1 by one laboratory) are also classified as major errors. It is worth noting at this stage that the presence of a myelodysplastic associated karyotypic abnormality should take diagnostic precedence over the detection of an NPM1 mutation (and also CEBPA). Other disorders categorised in this trial as major errors are T-lymphoblastic lymphoma/leukaemia and myelodysplastic/myeloproliferative neoplasms, unclassifiable. This case has not got a T-lineage phenotype and to be classified as the latter there has to be less than 20% blasts in the bone marrow and peripheral blood furthermore patients with an isolated del(5q) (as seen in this case) are excluded from this latter category.

It was concluded by the Steering Committee that the correct diagnosis was AML with myelodysplastic-related changes (with aberrant CD7 expression) even though that such cases are rare in children. This was on the basis that unbalanced chromosome abnormalities take precedence in categorisation of such cases over the purely morphological categories of AML, NOS. Thus, it was felt that all other diagnoses offered in this trial that fell into AML, NOS (AML with minimal differentiation, AML without maturation, AML with maturation, Acute megakaryoblastic leukaemia, Acute monoblastic and monocytic leukaemia and Acute myelomonocytic leukaemia) are considered as minor errors. However, it should be stated that 50% of the steering committee did consider that Acute monoblastic and monocytic leukaemia and Acute myelomonocytic leukaemia should be considered a major error and 50% considered that they should be classified as a minor error.

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Further Trial Findings

Table 1: Submissions from all participants - laboratories and individuals.

Diagnosis	Total No. of Returns	No. of Laboratories	No. of Individual
AML without maturation	116	84	32
AML with myelodysplasia-related changes	102	79	23
AML with minimal differentiation	61	37	24
AML with maturation	15	8	7
Acute monoblastic and monocytic leukaemia	4	3	1
Acute myelomonocytic leukaemia	3	1	2
Acute promyelocytic leukaemia with t(15;17)(q22;q12); PML-RARA	2	0	2
Therapy-related myeloid neoplasms	2	2	0
Acute megakaryoblastic leukaemia	1	1	0
T-lymphoblastic lymphoma/leukaemia	1	0	1
Myelodysplastic/myeloproliferative neoplasms, unclassifiable	1	0	1
AML with mutated NPM1	1	1	0

Table 2: Submissions from laboratory participants only

Diagnosis	Laboratory Returns %
AML without maturation	38.9
AML with myelodysplasia-related changes	36.6
AML with minimal differentiation	17.1
AML with maturation	3.7
Acute monoblastic and monocytic leukaemia	1.4
Acute myelomonocytic leukaemia	0.5
Therapy-related myeloid neoplasms	0.9
Acute megakaryoblastic leukaemia	0.5
AML with mutated NPM1	0.5

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Table 3: Submissions from individual participants only

Diagnosis	Individual Returns %
AML without maturation	34.4
AML with myelodysplasia-related changes	24.7
AML with minimal differentiation	25.8
AML with maturation	7.5
Acute monoblastic and monocytic leukaemia	1.1
Acute myelomonocytic leukaemia	2.2
Acute promyelocytic leukaemia with t(15;17)(q22;q12); PML-RARA	2.2
T-lymphoblastic lymphoma/leukemia	1.1
Myelodysplastic/myeloproliferative neoplasms, unclassifiable	1.1

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References:

1. Steven H. Swerdlow, Elias Campo, Nancy Lee Harris, Elaine S Jaffe, Stefano A. Pileri, Harald Stein, Jürgen Thiele, James W. Vardiman. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th Edition. IARC Press 2008

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Information with respect to compliance with standards BS EN ISO/IEC 17043:2010

4.8.2 a) The proficiency testing provider for this programme is:
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4.8.2 b) The coordinators of UK NEQAS LI programmes are Prof David Barnett and Mr Liam Whitby.

4.8.2 c) Person(s) authorizing this report:
Prof David Barnett, Director or Mr Liam Whitby, Operations Manager of UK NEQAS LI

4.8.2 d) No activities in relation to this EQA exercise were subcontracted.

4.8.2 g) The UK NEQAS LI Confidentiality Policy can be found in the Quality Manual which is available by contacting the UK NEQAS LI office. Participant details, their results and their performance data remain confidential unless revealed to the relevant NQAAP when a UK participant is identified as having performance issues.

4.8.2 i) All EQA samples are prepared in accordance with strict Standard Operational Procedures by trained personnel proven to ensure homogeneity and stability. Where appropriate/possible EQA samples are tested prior to issue. Where the sample(s) issued is stabilised blood or platelets, pre and post stability testing will have proved sample suitability prior to issue.

4.8.2 l), n), o), r) & s) Please refer to the UK NEQAS LI website at www.ukneqasli.co.uk for detailed information on each programme including the scoring systems applied to assess performance. Where a scoring system refers to the 'consensus result' this means the result reported by the majority of participants for that trial issue. Advice on the interpretation of statistical analyses and the criteria on which performance is measured is also given. Please note that where different methods/procedures are used by different groups of participants these may be displayed within your report, but the same scoring system is applied to all participants irrespective of method/procedure used.

4.8.2 m) We do not assign values against reference materials or calibrants.

4.8.2 q) Details of the programme designs as authorized by The Steering Committee and Specialist Advisory Group can be found on our website at www.ukneqasli.co.uk. The proposed trial issue schedule for each programme is also available.

4.8.2 t) If you would like to discuss the outcomes of this trial issue, please contact UK NEQAS LI using the contact details provided.

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